

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
3 November 2005 (03.11.2005)

PCT

(10) International Publication Number  
WO 2005/102305 A3

## (51) International Patent Classification:

C07C 261/00 (2006.01) C07C 229/00 (2006.01)  
C07C 69/76 (2006.01) A61K 31/40 (2006.01)

## (21) International Application Number:

PCT/US2005/013876

(22) International Filing Date: 22 April 2005 (22.04.2005)

(25) Filing Language:

English

(26) Publication Language:

English

## (30) Priority Data:

60/564,721 22 April 2004 (22.04.2004) US

(71) Applicant (for all designated States except US): ALLOS  
THERAPEUTICS, INC. [US/US]; 11080 Circle Point  
Road, Suite 200, Westminster, CO 80020 (US).

## (72) Inventors; and

(75) Inventors/Applicants (for US only): QUICK, AI  
[US/US]; 1525 South Lansing Street, Aurora, CO 80012  
(US). SANTOS, Antonio, M. [PT/US]; 6 Harvest Lane,  
Columbus, NJ 08022 (US). CARVALHO, Alexandre J.,  
G., G. [PT/PT]; Alameda Antonio Sergio 4-6A, P-1750  
Lisboa (PT). JOHNSON, Douglas, G. [US/US]; 6244  
Devinney Circle, Arvada, CO 80004 (US). ETTER,  
Jeffrey, B. [US/US]; 1318 Deer Trail Road, Boulder,  
CO 80302 (US). MURRAY, Chris [US/US]; 42 Summit  
Street, Arlington, MA 02474 (US).(74) Agents: SWANSON & BRATSCHE, L.L.C. et al.;  
1745 Shea Center Drive, Suite 330, Highlands Ranch, CO  
80129 (US).(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE,  
KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM,  
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,  
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,  
YU, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SI, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

## Published:

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:

10 August 2006

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS OF ALLOSTERIC HEMOGLOBIN MODIFIERS AND METHODS OF MAKING THE SAME

(57) Abstract: ABSTRACT The present invention provides novel compositions of allosteric hemoglobin modifiers which are substantially free of impurities, specifically polymeric impurities. In one embodiment, the novel compositions contain an allosteric hemoglobin modifier compound and less than 100 ppm of the polymeric impurities generated during the preparation of this compound. Included in the present invention are novel methods for preparing allosteric hemoglobin modifiers that are substantially free of polymeric impurities. Also included in the present invention are improved methods for the purification of the product formed by the method of this invention. The novel methods of purification comprise extracting the crude composition with a water immiscible or partially immiscible solvent such as methylisobutyl ketone (MIBK) to lower amounts of impurities, specifically polymeric impurities. Also included are methods to reduce impurities by recrystallization of the crude synthesized product, followed by filtration of the recrystallized product. The present invention also includes the products made by the processes of the invention and methods for analyzing compositions comprised of these products.